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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/511,430	08/18/2005	Guy D. Diana	1282-P02361US01	2400

110 7590 12/24/2009

DANN, DORFMAN, HERRELL & SKILLMAN
1601 MARKET STREET
SUITE 2400
PHILADELPHIA, PA 19103-2307

EXAMINER	
ROBINSON, BINTA M	

ART UNIT	PAPER NUMBER
1625	

MAIL DATE	DELIVERY MODE
12/24/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/511,430	DIANA ET AL.	
	Examiner	Art Unit	
	BINTA M. ROBINSON	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *Applicant arguments filed 11/25/09*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9 and 36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9, 36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/25/09 has been entered.

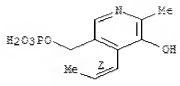
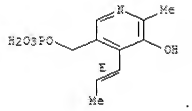
2. The 102 (b) rejection and 103 (a) rejections over Hcaplus 1977:52064, the 102 (b) rejection over Hcaplus 1989:186494, the 102 (b) rejection over Hcaplus 1974:129778, and the 103 (a) rejection over Hcaplus 1989:186494, and the 103 (a) rejection over Hcaplus 1974:129778 are withdrawn because of applicant's amendments filed 11/25/09.

3. (new rejections)

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1, 2, 4, 5, 7, and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hcaplus 1977:52064 further in view of Patani et. al.

Hcaplus 1977:52064 teaches the compounds  and  ; the instant compounds are bioisosteres of the prior art compounds.

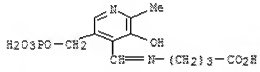
The difference between the Hcaplus 1977:52064 biosostere and the instantly claimed compound is in the instant compound, R is substituted methyl, that can be substituted with flourine, whereas in the prior art, the methyl is unsubstituted. The prior art compound and the instant compound are bioisosteres of each other. Bioisosteres are compounds that differ by an atom or radicals that share similar physiochemical properties and consequently two compounds that are bioisosteres of one another have similar biological activity, which may even be antagonistic. A fluorine atom, a methyl group, and an amino group are bioisosteric replacements for hydrogen. (See Patani, see page 3152). It would have been obvious to one of ordinary skill in the art to synthesize bioisosteres of this class of compounds. Accordingly, the compounds and compositions are deemed unpatentable therefrom in the absence of a showing of unexpected results for the claimed compounds and compositions over those of the prior art compounds.

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 1, 2, 4, 5, 7, and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hcaplus 1989:186494 further in view of Patani et. al.

Hcaplus 1989:186494 teaches the compound



and the instant compound is a bioisostere of the prior art compound.

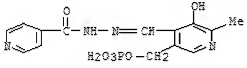
The difference between the Hcaplus 1989:186494 compound and composition and the instantly claimed compound is in the instant compound, R is a substituted methyl, that can be substituted with flourine, whereas in the prior art, the methyl is unsubstituted. The prior art compound and the instant compound are bioisosteres of each other. Bioisosteres are compounds that differ by an atom or radicals that share similar physiochemical properties and consequently two compounds that are bioisosteres of one another have similar biological activity, which may even be antagonistic. A fluorine atom, a methyl group, and an amino group are bioisosteric replacements for hydrogen. (See Patani, see page 3152). It would have been obvious to one of ordinary skill in the art to synthesize bioisosteres of this class of compounds. Accordingly, the compounds and compositions are deemed unpatentable therefrom in the absence of a showing of unexpected results for the claimed compounds and compositions over those of the prior art compounds.

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 1, 2, 4, 5, 7, and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hcaplus 1974:129778 further in view of Patani et. al.

Hcaplus 1974:129778 teaches the compound



and the instant compound is a bioisostere of the prior art compound.

The difference between Hcaplus 1974:129778 compound and composition and the instantly claimed compound is in the instant compound, R is a substituted methyl, that can be substituted with flourine, whereas in the prior art, the methyl is unsubstituted. The prior art compound and the instant compound are bioisosteres of each other. Bioisosteres are compounds that differ by an atom or radicals that share similar physiochemical properties and consequently two compounds that are bioisosteres of one another have similar biological activity, which may even be antagonistic. A fluorine atom, a methyl group, and an amino group are bioisosteric replacements for hydrogen. (See Patani, see page 3152). It would have been obvious to one of ordinary skill in the art to synthesize bioisosteres of this class of compounds. Accordingly, the compounds and compositions are deemed unpatentable therefrom in the absence of a showing of

unexpected results for the claimed compounds and compositions over those of the prior art compounds.

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 1-9, 36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

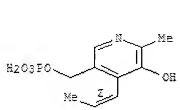
12. A. In claim 1, line 21, page 3, and all other occurrences throughout the claims, the phrase "isomeric forms of said compound" is unclear because it is indefinite and unclear as to what compounds are being claimed. By definition an isomer can be compounds with the same molecular formula, but different arrangements of atoms in space. Isomers differ in properties because of differences in the arrangement of atoms.

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

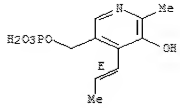
> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claim 36 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hcaplus 1977:52064 further in view of Patani et. al. and in view of Zitzmann et. al.

Hcaplus 1977:52064 teaches the compositions containing compounds



and



for treating at least one infection caused by virus of the flaviviridae family in combination with ribavirin; the non-ribavirin compound component of the instant composition is a bioisostere of the prior art compounds. The difference between the Hcaplus 1977:52064 biosostere and the instantly claimed compound is in the instant compound, R is substituted methyl, that can be substituted with flourine, whereas in the prior art, the methyl is unsubstituted. The prior art compound and the instant compound are bioisosteres of each other. Bioisosteres are compounds that differ by an atom or radicals that share similar physiochemical properties and consequently two compounds that are bioisosteres of one another have similar biological activity, which may even be antagonistic. A fluorine atom, a methyl group, and an amino group are bioisosteric replacements for hydrogen. (See Patani, see page 3152). Zitzmann et. al. teaches that ribavirin can be used in combination with other therapies such as IFN-alpha therapy, known for treating viruses of the Flaviviridae family. See page 11878, second paragraph of Zitzmann et. al. It would have been obvious to one of ordinary skill in the art to synthesize compositions containing bioisosteres of this class of compounds and also containing ribavirin to treat at least one infection caused by virus of the Flavivirdae family and disease associated with said infenction. Accordingly, the compositions are deemed unpatentable therefrom

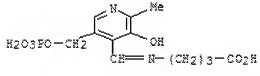
in the absence of a showing of unexpected results for the claimed compositions over those of the prior art compounds.

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

16. Claim 36 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hcaplus 1989:186494 further in view of Patani et. al. and Zitzmann et. al.

Hcaplus 1989:186494 teaches the composition containing the compound



in combination with ribavirin,

for treating at least one of infection caused by virus of the flaviviridae family in combination with ribavirin; the non-ribavirin compound component of the instant composition is a bioisostere of the prior art compounds. The difference between the Hcaplus 1989:186494 biosostere and the instantly claimed compound is in the instant compound, R is substituted methyl, that can be substituted with flourine, whereas in the prior art, the methyl is unsubstituted. The prior art compound and the instant compound are bioisosteres of each other. Bioisosteres are compounds that differ by an atom or radicals that share similar physiochemical properties and consequently two compounds that are bioisosteres of one another have similar biological activity, which may even be antagonistic. A fluorine atom, a methyl group, and an amino group are bioisosteric

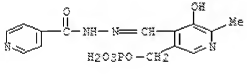
replacements for hydrogen. (See Patani, see page 3152). Zitzmann et. al. teaches that ribavirin can be used in combination with other therapies such as IFN-alpha therapy, known for treating viruses of the Flaviviridae family. See page 11878, second paragraph of Zitzmann et. al. It would have been obvious to one of ordinary skill in the art to synthesize compositions containing bioisosteres of this class of compounds and also containing ribavirin to treat at least one infection caused by virus of the Flavivirdae family and disease associated with said infection. Accordingly, the compositions are deemed unpatentable therefrom in the absence of a showing of unexpected results for the claimed compositions over those of the prior art compounds.

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

18. Claim 36 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hcaplus 1974:129778 further in view of Patani et. al. and Zitzmann et. al.

Hcaplus 1974:129778 teaches the composition containing the compound,



in combination with ribavirin and the non-ribavirin compound component of the composition, is a bioisostere of the prior art compound. The difference between Hcaplus 1974:129778 non-ribavirin compound and the instantly claimed compound is in the instant compound, R is a substituted methyl,

that can be substituted with flourine, whereas in the prior art, the methyl is unsubstituted. The prior art compound and the instant compound are bioisosteres of each other. Bioisosteres are compounds that differ by an atom or radicals that share similar physiochemical properties and consequently two compounds that are bioisosteres of one another have similar biological activity, which may even be antagonistic. A fluorine atom, a methyl group, and an amino group are bioisosteric replacements for hydrogen. (See Patani, see page 3152). Zitzmann et. al. teaches that ribavirin can be used in combination with other therapies such as IFN-alpha therapy, known for treating viruses of the Flaviviridae family. See page 11878, second paragraph of Zitzmann et. al. It would have been obvious to one of ordinary skill in the art to synthesize compositions containing bioisosteres of this class of compounds and also containing ribavirin to treat at least one infection caused by virus of the Flaviviridae family and disease associated with said infection. Accordingly, the compositions are deemed unpatentable therefrom in the absence of a showing of unexpected results for the claimed compositions over those of the prior art compounds.

Response to Applicant's remarks

The applicant's amendment overcame the 102 and 103 rejections of record in the office action filed 5/29/09. The applicant traverses the 103 rejections of claims 2, 5, and 8 with regard to pharmaceutical compositions alleging that the references do not disclose the phrase "pharmaceutically acceptable carrier medium". This phrase does not lend patentable weight to these claims, because these media are not active compounds, but inert carriers. It would be obvious to add a pharmaceutically

acceptable carrier to a known compound, or an obvious compound, and this is why the 103 (a) rejections above were made.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Binta M. Robinson whose telephone number is (571) 272-0692. The examiner can normally be reached on M-F (9:30-6:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0670.

A facsimile center has been established. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier numbers for accessing the facsimile machine are (703)308-4242, (703305-3592, and (703305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571)272-1600.

/Binta M Robinson/

Examiner, Art Unit 1625

/Janet L. Andres/

Supervisory Patent Examiner, Art Unit 1625